UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/993,669	11/27/2001	Ann-Kristin Karlsson	06275-160002	1605

26161 7590 03/25/2003

FISH & RICHARDSON PC
225 FRANKLIN ST
BOSTON, MA 02110

EXAMINER	
MAIER, LEIGH C	12

ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 03/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/993,669	Applicant(s) Karlsson
	Examiner Leigh Maier	Art Unit 1623

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jan 9, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *3, 4, 6, 8-12, 14, and 30-54* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *3, 4, 6, 8-12, 14, and 30-54* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

Claim 55 has been canceled. Claims 3, 8, 10, 11, 39, and 50 have been amended. Claims 3, 4, 6, 8-12, 14, and 30-54 are pending. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Any objection or rejection not expressly repeated has been withdrawn.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 9, 2003 has been entered.

Claim Objections

Claims 36 and 53 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claims, or amend the claims to place the claims in proper dependent form, or rewrite the claims in independent form.

Regarding claim 36, the claim requires a powder suitable for inhalation. It depends from claim 3 which has been amended to require an "inhalation powder."

Regarding claim 53, the claim recites that "the formulation is a suspension." It depends from claim 8 which has been amended so that "formulation" has been changed to "suspension."

Claim Rejections - 35 U.S.C. § 103

Claims 3, 4, 6, 34-36, 39, 41, 42, 45-47, and 49-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) and BUSSEY et al (J. Parenter. Sci. Tech., 1983).

Independent claim 3 has been amended to require a pharmaceutically acceptable inhalation powder comprising a glucocorticosteroid in the form of sterile, dry finely divided particles. The claim recites that the particles be heat sterilized. Dependent claims recite limitations regarding particle size and purity.

Independent claim 39 has been amended to require a pharmaceutically acceptable inhalation powder comprising a glucocorticosteroid in the form of sterile, finely divided particles. The claim recites that the particles be heat sterilized. Dependent claims recite limitations regarding particle size and conditions for heat sterilization.

Independent claims 49-52 are drawn to heat-sterilized glucocorticosteroid products, similar to those described above.

JAKUPOVIC teaches a crystalline form of the anti-inflammatory agent, budesonide, in which 90% of the particles have a diameter of less than 5.7 μm, for nasal inhalation in treating diseases of the respiratory tract. See example 1, page 8 and page 4, lines 4-6. The reference further teaches a particle range of about 0.1 μm to about 10 μm. See paragraph bridging pages 3 and 4. The reference also teaches the use of other glucocorticosteroids, such as rofleponide and mometasone. The reference further teaches the preparation of pharmaceutical compositions by adding any of a variety of pharmaceutically acceptable carriers. See page 5, beginning line 11, continuing through page 6, line 17.

JAKUPOVIC does not teach a sterile product. The reference further does not teach the percentage by weight of the glucocorticosteroid.

BUSSEY teaches the sterilization of (gluco)corticosteroid powders by ^{60}Co irradiation. See entire reference, particularly the abstract. The claim also teaches that ethylene oxide is used to sterilize bulk steroids. See introduction.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to sterilize the respirable, dry powders disclosed by JAKUPOVIC by either irradiation or treatment with ethylene oxide. The artisan would have been motivated to sterilize the respirable particles to prevent microbial growth in the packaged material with a reasonable expectation of success. The artisan would be particularly motivated to sterilize the glucocorticosteroid in the form which it is intended to be used.

It would also be obvious to the ordinarily skilled worker to purify the glucocorticosteroid (prepare in a form having a high percentage of the glucocorticosteroid by weight) in order to limit contaminants in products for human administration.

It would be further obvious to prepare pharmaceutical compositions for their art-disclosed utility, as described by JAKUPOVIC.

Applicant contends that "[n]othing in Jakupovic suggest or provides motivation to produce an inhalation powder is [sic] in the form of finely divided particles, the particles being heat sterilized." JAKUPOVIC clearly teaches inhalation powders. See page 3, lines 23-25: "Where *the powder is intended particularly for oral inhalation*, preferably the particles have a mass median diameter of 10 μm or less, preferably 7 μm or less." (Emphasis added) One of ordinary skill would be motivated to sterilize the powder for reasons discussed above.

Applicant further contends that one of ordinary skill would not be motivated by the art of record to heat sterilize an inhalation powder. The examiner agrees that the art of record would not teach a *process* to heat sterilize an inhalation powder. However, the claims are drawn to products which comprise a product-by-process, and determination of patentability is based on the product itself. *The patentability of a product does not depend on its method of production.* If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.

Regarding Applicant's contention the "heat sterilization gave superior results to irradiation sterilization." Again, this would be relevant to a claim drawn to a method of heat

sterilization. It may be that heat sterilization allows for the preparation of a sterile product of greater purity than the maximum purity that can be obtained from irradiation sterilization. If that showing can be made, then a claim with a minimum purity limitation (supported by the specification) may be allowable. The data in Table 8 does not support such a claim because the data does not necessarily show the maximum purity that can be achieved with an irradiation protocol, as the starting (pre-irradiation) purity of the budenoside is not disclosed.

Claims 8-12, 14, 30, 31, 43, 44, 48, 53, and 54 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) and BUSSEY et al (J. Parenter. Sci. Tech., 1983) as applied to claims 3, 4, 6, 34-36, 39, 41, 42, 45-47, and 49-52 above, in view of SEQUIEIRA et al (US 5,837,699).

The invention is as set forth above. Dependent claims recite methods of treating specific respiratory disorders by administering the sterile glucocorticosteroid and concentrations of the pharmaceutical compositions comprising the sterile glucocorticosteroid.

Independent claim 8 has been amended to require a pharmaceutical suspension comprising a glucocorticosteroid of essentially the same form as that recited in claim 3. Dependent claims recite limitations regarding particle size, purity, and the preparation of pharmaceutical compositions using the sterile glucocorticosteroid.

Independent claim 54 is drawn to a suspension comprising sterilized budesonide or rofleponide.

JAKUPOVIC teaches as set forth above. The reference teaches treatment of diseases of the respiratory tract in general, but not the particular disorders recited in the claims. The reference teaches the preparation of pharmaceutical compositons, but not specifically suspensions.

BUSSEY teaches as set forth above.

SEQUIEIRA teaches nasal inhalation of a number of (gluco)corticosteroids including budesonide and mometasone for the treatment of specific respiratory disorders, such as COPD, asthma, and rhinitis. See col 1-2. The reference further teaches administration of the glucocorticosteroid as a dry powder or as an aqueous suspensions of about 0.01 to about 10 mg of glucocorticosteroid to gram of suspenstion. See col 5. Given that 1g water = 1ml water, this range is approximately the same as the concentrations (mg/ml) recited in the claims.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to use the dry, sterile glucocorticosteroids or as aqueous suspensions of said glucocorticosteroids for the treatment of the recited respiratory disorders for their art-disclosed utility. It would be within the scope of the artisan to optimize the dosage and prepare suspensions of appropriate concentration for said dosage through routine experimentation.

Claims 32, 33, and 40 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) and BUSSEY et al (J. Parenter. Sci. Tech., 1983) as applied

to 3, 4, 6, 34-36, 39, 41, 42, 45-47, and 49-52 above, and in further view of RADHAKRISHNAN et al (US 5,192,528).

The invention is as set forth above. Dependent claims further limit the particle size.

JAKUPOVIC teaches as set forth above. The aim of the reference is preparation of glucocorticosteroids available to the lower respiratory tract. See page 1, lines 9-15. As noted above, JAKUPOVIC teaches the range of particles of about 0.1 μm to about 10 μm, but the reference does not specifically exemplify particles of less than 5 μm. However, the reference teaches how the size of the particles may be controlled by process parameters that one of ordinary skill would be able to optimize with routine experimentation.

BUSSEY teaches as set forth above.

RADHAKRISHNAN teaches that aerosol particles of corticosteroid formulations must be must be less than about 1 μm in order to reach the lower region of the respiratory tract (alveoli). See figure 1; col 5, lines 37-48; and col 7, lines 57-63.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare glucocorticosteroid in the form of sterile, respirable particles with MMD of less than 1 μm. The artisan would have been motivated to prepare this size in order for the respirable glucocorticosteroid to reach the alveoli during treatment with a reasonable expectation of success. The artisan would be motivated to sterilize the product for reasons described above.

Claims 8, 11, and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over JAKUPOVIC et al (WO 96/32095) and BUSSEY et al (J. Parenter. Sci. Tech., 1983) as applied to claims 3, 4, 6, 34-36, 39, 41, 42, 45-47, and 49-52 above, in view of SEQUIEIRA et al (US 5,837,699) and RADHAKRISHNAN et al (US 5,192,528).

The invention is as set forth above. Claim is drawn to a suspension of concentration recited in claim 11, wherein the particles have MMD of less than 4 μm.

JAKUPOVIC and BUSSEY teach as set forth above. The references do not teach a suspension comprising sterile particles wherein the particles have MMD of less than 4 μm.

SEQUIEIRA and RADHAKRISHNAN teach as set forth above.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to prepare sterile powder and prepare a suspension as set forth above. One of ordinary skill would be motivated to prepare a suspension comprising particles having MMD of less than 4 μm because SEQUIEIRA had taught the utility of these glucocorticosteroids in suspension for the treatment of a number of respiratory disorders, and RADHAKRISHNAN had taught that particles of this size are necessary for delivering the compounds to the lower respiratory tract. These suspensions are taught in dosage levels suggesting concentrations embraced by that recited in the claims.

Examiner's hours, phone & fax numbers

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leigh Maier whose telephone number is (703) 308-4525. The examiner can normally be reached on Tuesday, Wednesday, or Friday 7:00 to 3:30 (ET).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. James O. Wilson (703) 308-4624, may be contacted. The fax phone number for Group 1600, Art Unit 1623 is (703) 308-4556 or 305-3592.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-1235.

Visit the U.S. PTO's site on the World Wide Web at http://**www.uspto.gov**. This site contains lots of valuable information including the latest PTO fees, downloadable forms, basic search capabilities and much more.

Leigh C. Maier
Patent Examiner
March 21, 2003